modeled electronically, in the electronic domain, by electronic hybridization machine 116, which produces a hybridization output (HYBRIDIZATION OUTPUT) 124 representative of information resulting from a hybridization reaction between first molecule 110 and second molecule 118. The invention is not intended to be limited to hybridization reactions, which are described herein for purposes of illustration. The invention may be expanded or adapted to other types of sequence analysis reactions in accordance with the present invention as described herein.

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REMARKS

Attorney Docket No.

Please note that the correct attorney docket number is DTR 112, not "DFTR 112". Thank you.

Change of Art Unit

The applicant notes that the art unit for the present application has been changed to Art Unit 1631. Thank you.

Response to Restriction Requirement

The examiner indicated that applicant's response to the restriction requirement was persuasive, and as a result the restriction requirement has been withdrawn. All claims 1-30 are under consideration and examination. Thank you.

Claims Rejections – 112

The examiner rejected claims 1-30 under 35 U.S.C. § 112, ¶ 2, as being indefinite. Regarding *"electronic hybridization"*, the examiner argued that the phrase renders claims 1-13, 15-22, and 30, indefinite. The applicant traverses the rejection for the following reasons.

The examiner based the section 112, second paragraph, rejection on the recited term *"electronic hybridization"* assay, however, this term does not appear in independent claim 23 and its dependent claims 24-25, nor does it appear in independent claim 26 and its dependent claims 27-30. Applicant kindly notes that the examiner appears to be mistaken with regard to the recitation of the term *"electronic hybridization"* assay in claim 30, as the term does not appear in said claim 30.

Thus, the rationale for the rejection based upon the term *"electronic hybridization"* assay does not apply to said claims 23-30. As a result, a *prima facie* indefiniteness rejection for said claims 23-30 was not set forth by the examiner. The applicant kindly urges the examiner to withdraw the 112, second paragraph, rejection of claims 23-30.

Regarding claims 1-22 with respect to the recitation of the term "electronic hybridization" assay and indefiniteness, the applicant responds as follows. The applicant kindly submits that patent which the examiner cites does not support the examiner's rejection. Said patent 5,849,486 to Heller et al. is merely directed to *"electrically controlled hybridization"* where the hybridization referred in said patent occurs as a chemical reaction by two molecules, not as an *"electronic hybridization"* reaction as defined in the specification and as recited in the applicant's claims. This conclusion is clear from a reading of the applicant's specification (for example, page 6 of the applicant's specification) and a reading of said patent to Heller et al. In fact, an electronic search of the text of said patent number 5,849,486 as downloaded from the Patent Office Internet site was executed by the applicant, and it was determined that the phrase *"electronic hybridization"* does not exist in said patent to Heller. Therefore, it is respectfully submitted that said patent to Heller et al. is not informative on the issue of whether the recited phrase *"electronic hybridization"* renders the claims indefinite.

The applicant submits that, contrary to the examiner's assertion, the phrase *"electronic hybridization"* does not render the claims indefinite under 35 U.S.C., second paragraph. The applicant further submits that the claimed invention as directed to an

"electronic hybridization" is novel and unobvious, and is a phrase utilized by the applicant under the legal concept that the applicant is entitled to be his own lexicographer:

> A fundamental principle contained in 35 U.S.C. 112, second paragraph is that applicants are their own lexicographers. They can define in the claims what they regard as their invention essentially in whatever terms they use so long as the terms are used in ways that are contrary to accepted meanings in the art. MPEP 2173.01

Since the examiner did not point to the actual existence of the term *"electronic hybridization"* anywhere in the art, it follows that this term as recited by the applicant cannot be contrary to any accepted meanings in the art because the term does not exist in the art. In fact, the applicant submits that, in accordance with the above mentioned fundamental principle that the applicants are the own lexicographer, the term *"electronic hybridization"* is a new term in the art and must be given weight as such in the balance of the 112, second paragraph, analysis:

> New terms are often used when a new technology is in its infancy or is rapidly evolving. The requirements for clarity and precision must be balanced with the limitations of the language and the science. If the claims, ***read in light of the specification***, reasonably apprise those skilled in the art both of the utilization and the scope of the invention, and of the language is as precise as the subject matter permits, the statute (35 U.S.C. 112, second paragraph) demands no more. MPEP 2173.05(a). (Emphasis added).

Thus, the new phrase *"electronic hybridization"* will be understood by those having skill in the art *when the applicant's specification is read at least in part or in its entirety*. As a result, it is urged that the rejection be withdrawn. Examples of a reading of the specification are as follows:

The specification provides a definition of *"electronic hybridization"* as recited in the claims. Fore example, the examiner's attention is kindly directed to page 3 of the applicant's specification:

> The ***electronic hybridization reaction***, generally referred to as a sequence analysis, performed by electronic hybridization machine 116 is in one embodiment of the invention ***representative of an actual chemical reaction*** between the physical forms of first molecule 110 and second molecule 118. In a physical world chemical hybridization reaction between first molecule 110 and second molecule 118, the extent to which the two molecules bind to one another is typically indicated with a reporter molecule such as a radioactive fluorescent reporter molecule. The greater the similarity between the two molecules, the greater the amount of binding between the two chemicals, resulting in a fluorescence or radioactive intensity of a signal provided by the reporter molecule. The intensity of the reporter molecule is usually observed by the human eye, or by a detector sensitive to the fluorescence or radioactivity of the reporter molecule. ***With the present invention, such a hybridization reaction is modeled electronically, in the electronic domain, by electronic hybridization machine*** 116, which produces a hybridization output (HYBRIDIZTION OUTPUT) 124 representative of information resulting from a hybridization reaction between first molecule and second molecule 118. (Emphasis added).

Thus, it is respectfully submitted that the above-cited paragraph directly contradicts the examiner's statement in the rejection: "Therefore, said expression is vague and indefinite as to whether the actual chemical or physical hybridization is included or whether 'only' virtual or software hybridization is meant thereby." In fact, it is respectfully submitted that the examiner contradicted the rejection by citing to said patent to Heller which is directed to a "device to *electrophoretically transport charged entities* for hybridization." (Emphasis added). It should be apparent upon a reading of the applicant's specification that electronic modeling of a hybridization assay in the electronic domain differs from electrophoresis of charged entities.

On page 6 of the applicant's specification:

> The invention provides the capability to implement a molecular hybridization reaction assay or the like without requiring an actual chemical reaction. ***The hybridization reaction is effectively implemented by a machine such as a computer, a hardware device, or a digital signal processor*** to provide the speed, flexibility, and capability of repetition of

> the same assay without requiring new materials to execute the assay. (Emphasis added).

Furthermore, FIGS. 5, 6, 7, and 8, and the corresponding discussion thereof, provide an exhaustive discussion of an electronic hybridization assay in accordance with the invention. For example:

On page 10 of the applicant's specification:

> Referring now to FIG. 5, a flow diagram of a method for implementing an electronic hybridization assay in accordance with the present invention will be discussed.

On page 13 of the applicant's specification:

> In accordance with one embodiment of the present invention, ***electronic hybridization machine 116 implements a correlation signal processing algorithm to determine the similarity between the sequences wherein a correlation output is representative of the degree of similarity between the sequences. The correlation algorithm may be executed by a general purpose computer, hardware correlator device, or by a digital signal processor, comparator, etc., or a combination thereof.*** (Emphasis added).
>
> In accordance with the present invention, ***the correlation algorithm is a mathematical operation that receives two sequences as an input and provides a correlation output value or sequence of values as an output.*** (Emphasis added).

The above-cited passages are not intended to be exhaustive, but show that the specification supports the definiteness of the term *"electronic hybridization"*. Therefore, the applicant respectfully submits that the specification contradicts the arguments set forth by the examiner for the 112, second paragraph, rejection based on the definiteness of the term *"electronic hybridization"*. It is therefore respectfully urged that the rejection be withdrawn.

RECITATION OF "COMPRISING" IN CLAIM 27, LINE 2

The examiner rejected claim 27, line 2 under 35 U.S.C. 112, second paragraph as reciting the term "comprising". The applicant respectfully traverses this rejection as having no legal basis, and as not being prohibited by 35 U.S.C. 112, second paragraph. In other words, the applicant respectfully submits that the examiner has failed to set forth a legal basis for requiring an applicant to change claim terminology from "comprising" to "consisting of". Furthermore, requiring such a change from "comprising" to "consisting of" may be considered inconsistent with the rights provided to applicants by congress under 35 U.S.C. 112, paragraph 6. In addition, the applicant kindly points out that claim 27 is directed to an apparatus for which the term "comprising" is extensively used in claims drafting, and not to a chemical compound where the term "consisting of" has been traditionally used as a claim drafting tool. As such, the applicant traverses the rejection and kindly requests the examiner to cite to a section of the MPEP, CFR, or appropriate federal case, which would support the requirement for the change, or otherwise withdraw the rejection.

CLAIM 29

Claim 29 has been amended herein to correct a minor typographical error, changing "one or more parallel channels" to --two or more parallel channels--.

Claim Rejections – 102

The examiner rejected claims 1-16 and 23-30 under 35 U.S.C. § 102(b) as being anticipated by Rothberg et al. (5,871,697).

ELECTRONIC HYBRIDIZATION

Regarding independent claim 1, contrary to the examiner's assertion, Rothberg does not disclose *"executing an electronic hybridization assay"* as claimed in independent claim 1 and its dependent claims 2-6. The examiner is kindly reminded that,

> A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. MPEP § 2131.01

> The identical invention must be shown in as complete detail as in the . . . claim. MPEP § 2131.01

Thus, Rothberg does not disclose or describe the identical invention as claimed by the applicant since Rothberg does not disclose executing an *"electronic hybridization"* assay. To the contrary, a computer search of the text of said patent to Rothberg as downloaded from the USPTO Internet site was performed by the applicant, and neither the word *"electronic"* nor the term *"electronic hybridization"* was found to exist in Rothberg. In fact, all of the hybridization reactions described by Rothberg are directed to chemical hybridization reactions, not electronic hybridization reactions. For example, in the Abstract, lines 1-4;

> The invention provides methods by which *biologically derived DNA* sequences in a *mixed sample* or in an *arrayed single sequence clone* can be determined and classified without sequencing. (Emphasis added).

In col. 4, lines 62-66:

> The signals are preferably optical, generated by *fluorochrome labels* and detected by automated optical detection technologies. Using these methods, multiple individually labeled moieties can be discriminated even though they are in the same *filter spot* or *gel band*. (Col. 4, lines 62-66). (Emphasis added).

In col. 5, lines 8-28

> DNA and PNA oligomers recognize their specific subsequences by hybridization methods.

In col. 6, lines 58-60, Rothberg describes:

> real-time detection of *DNA hybridization* and melting on *oligonucleotide arrays* by using optical waveguides (Emphasis added).

Again in the Abstract:

> Computer implemented methods are provided *to analyze the experimental results* and to determine the sample sequences in question and to carefully choose target subsequences in order that *experiments* yield a maximum amount of information.

Clearly, Rothberg discusses generating signals *after a chemical hybridization* reaction, but does not teach an *"electronic hybridization"* reaction as claimed by the applicant. Where any hybridization is discussed by Rothberg, Rothberg's invention is directed to analysis of the results of a chemical hybridization reaction, not an *"electronic hybridization"* reaction as claimed by the applicant. None of the computer analysis cited by the examiner is directed to an electronic hybridization reaction. For example, the examiner cited to column 70, lines 37-46, but failed to cite to the immediately preceding two sentences in col. 70 sentence which demonstrate that the passage cited by the examiner is discussing the results of chemical hybridization reaction:

> This embodiment is directed to gene determination and classification of *arrayed samples or colonies*, where each sample or colony contains or expresses only one sequence or gene of interest and is perhaps *prepared from a tissue cDNA library*. The presence or absence of target subsequences in a colony is determined by use of *labeled hybridization* recognition means, each of which *uniquely binds* to one target subsequence. (Col. 70, lines 29-37. (Emphasis added).

These two sentences illustrate that what Rothberg is discussing is a typical chemical hybridization reaction. Furthermore, the recitation of the word "then" in the cited sentence of "Each sample is then characterized by a hash code . . ." shows that any computer steps discussed by Rothberg occur after any chemical hybridization reaction, and does not teach an *"electronic hybridization"* reaction.

As a result, Rothberg does not teach an *"electronic hybridization"* reaction or assay and is *prima facie* insufficient to support an anticipation rejection. It is therefore urged that the rejection be withdrawn for this and all rejections based upon the patent to Rothberg as discussed herein.

Likewise, regarding independent claim 7, contrary to the examiner's assertion, Rothberg does not disclose *"means for executing an electronic hybridization assay"* as claimed in independent claim 7 and its dependent claims 8-16.

Likewise, regarding independent claim 17, contrary to the examiner's assertion, Rothberg does not disclose a machine readable medium having a program of instructions stored thereon, the program of instructions for causing a machine to implement steps for executing an electronic hybridization assay according to the program of instructions, including *"executing an electronic hybridization assay"* as claimed in independent claim 17 and its dependent claims 18-22.

WHEREIN THE FIRST SEQUENCE INCLUDES AT LEAST ONE POSITIVE VLUE AND AT LEAST ONE NEGATIVE VALUE

Contrary to the examiner's assertion, the patent to Rothberg does not disclose executing an electronic hybridization assay, or means for executing an electronic hybridization assay *"wherein the first sequence includes at least one positive value and at least one negative value"* as claimed in claims 3, 13, and 19. In fact, the examiner never addressed this limitation anywhere in the entire office action.

ELECTRONIC HYBRIDIATION MACHINE

Contrary to the examiner's rejection, the patent to Rothberg does not disclose *"an electronic hybridization machine"* as claimed in claim 8.

DIGITAL SIGNAL PROCESSOR STRUCTURE

Contrary to the examiner's rejection, the patent to Rothberg does not disclose *"a digital signal processor structure"* as claimed in claims 10, nor correlating means comprising a digital signal processor as claimed in claim 27. For example, please refer to page 8, lines 4-9, the discussion of FIG. 3, etc. for a discussion of a digital signal processor. In fact, the examiner never addressed this limitation anywhere in the entire office action.

HARDWARE CORRELATOR DEVICE STRUCTURE

Contrary to the examiner's rejection, the patent to Rothberg does not disclose *"a hardware correlator device structure"* as claimed in claim 11, nor correlating means comprising a hardware correlator as claimed in claim 27. For example, please refer to page 10, lines 20-29, of the specification for a sample discussion of a hardware correlator.

OPTIMIZATION

Regarding the rejection of claims 2-3 and 23-25, since the patent to Rothberg does not disclose an *"electronic hybridization"* reaction, it follows that Rothberg cannot teach optimizing an *"electronic hybridization"*. Rothberg only teaches optimizing an experiment, but not any *"electronic hybridization"*, contrary to the examiner's assertion. The same holds true for the rejection of claims12-13.

PERFORMING A CORRELATION ALGORITHM

Regarding claims 4 and 14, and also claims 20, 23, 26, and 27, the examiner cited to a passage in Rothberg directed to a step to "perform statistical correlations". It should be noted that this reference to a statistical correlation is discussed in a generic sense and definition of the word "correlation". The cited passage does not teach performing a correlation algorithm as claimed by the applicant and as defined in the specification. The examiner's attention is kindly directed to the applicant's specification, on page 14 which defines the mathematical correlation algorithm formula and which provides a sample FORTRAN programming language implementation of such a correlation algorithm. As discussed in the applicant's specification, a correlation algorithm is an operation that may provide an output representative of the degree of similarity of two sequences. Such a definition of a correlation algorithm is provided in the signal processing discipline of electrical engineering, and as such is consistent with the term correlation as known to the art of electrical engineering signal processing. Thus, the reference to "correlation". in Rothberg is not identical to the recitation of "correlation" in the applicant's claims.

PARALLEL CHANNELS FOR EXECUTING AT ELAST ONE OR MORE CORRELATION ALGORITHMS SIMULTANEOUSLY

Regarding the rejection of claim 29, it is respectfully submitted that the examiner failed to consider the entirety of the claim, and only focused on the word parallel. Claim 29 (as amended herein) recites:

> said means for correlating including at least two or more parallel channels for performing at least two or more correlation algorithms simultaneously, one correlation algorithm for each channel.

The passage cited by the examiner merely refers to parallelizing signal detection, but fails to make any mention of a "correlation algorithm", and so is not identical to the applicant's claimed invention.

MULTIPLY AND ACCUMULATE

Regarding claims 25 and 29, Rothberg does not teach *"said correlating step including a multiply and accumulate operation"* or *"said correlating means including means for executing a multiply and accumulate operation"* as claimed in claims 25 and 29, nor did the examiner attempt to point to such multiply and accumulate operation in the patent to Rothberg. In fact, the examiner never addressed this limitation anywhere in the entire office action.

Since it is respectfully submitted that the patent to Rothberg does not disclose anything that is identical to the applicant's claimed invention, as required by the statute, Rothberg does not anticipate the applicant's claims. It is therefore urged that the section 102 rejection be withdrawn.

Claim Rejections – 103

ASHLEY (Claims 1-6)

The examiner rejected claims 1-6 under 35 U.S.C. § 103(a) as being unpatentable over Ashley (J.Am.Chem.Soc. 1992, Vol. 144, No. 25, pages 9731-9736) in view of Rothberg.

Applicant kindly points out that neither reference teaches an *"electronic hybridization"* as disclosed and claimed by the applicant. Ashley does not disclose any formula or other basis for the cited "DNA modeling calculations". Furthermore, there is no teaching in Ashley that the modeling calculations were performed using an *"electronic hybridization"* technique as disclosed and defined by the applicant. As discussed with respect to the 102 rejection, above, Rothberg does not teach all of the claimed elements of the applicant's claims. Furthermore, the combination of Ashley and Rothberg does not teach all of the elements of the invention, nor an *"electronic hybridization"* as disclosed and claimed by the applicant.

The examiner is kindly reminded that, in order to support a *prima facie* obviousness rejection, three basic criteria must be met (MPEP §§ 2142 and 2143):

1. The prior art reference (or references when combined) must teach or suggest all the claim limitations;
2. There must be some suggestion or motivation to modify the reference or to combine the reference teachings.
3. There must be a reasonable expectation of success.

Furthermore, as discussed with respect to the 102 rejection, Rothberg is only directed to computer methods to analyze the experimental results of chemical reactions, after the reaction as occurred, and not to implement an *"electronic hybridization"* reaction as claimed by the applicant. As such, Rothberg teaches away from an *"electronic hybridization"* reaction since all of Rothberg only discloses chemical hybridizations, and also because the computer implemented analysis in Rothberg occurs *after* the reaction, not as any part of an actual reaction. This teaching away argument applies to all of the 103 rejections that are based on the patent to Rothberg.

Regarding claim 3, neither Ashley nor Rothberg teaches *"wherein the first sequence includes at least one positive value and at least one negative value"* as claimed in claim 3. In fact, the examiner never addressed this limitation anywhere in the office action.

Regarding claim 4, neither Ashley nor Rothberg teaches *"the step of performing a correlation algorithm on the first sequence and the reference sequence, the output of said providing step including a correlation output"* as claimed in claim 4.

It is therefore believed that for the above reasons, a *prima facie* case of obviousness was not established. Therefore, the rejection should be withdrawn.

MITSUHASHI (Claims 7-16)

The examiner rejected claims 7-16 under 35 U.S.C. § 103(a) as being unpatentable over Mitsuhashi (5,556,749) in view of Rothberg.

Neither Mitsuhashi nor Rothberg teaches means for executing an *"electronic hybridization"* assay as claimed by the applicant in claim 7 and its dependent claims 8-16, and as defined in the applicant's specification. A computer text search of the patent to Mitsuhashi was performed, and neither the term *"electronic"* nor the term *"electronic hybridization"* were found to exist therein. Therefore, a *prima facie* rejection was not set forth.

Regarding claim 10, neither Mitsuhashi nor Rothberg teaches a *"digital signal processor structure"* as claimed in claim 10. In fact, the examiner never addressed this limitation anywhere in the entire office action.

Regarding claim 11, neither Mitsuhashi nor Rothberg teaches a *"hardware correlator device structure"* as claimed in claim 11.

Regarding claim 13, neither Mitsuhashi nor Rothberg teaches *"wherein the first sequence includes at least one positive and one negative value"* as recited in claim 13. In fact, the examiner never addressed this limitation anywhere in the office action. In fact, the examiner never addressed this limitation anywhere in the entire office action.

Regarding claim 14, neither Mitsuhashi nor Rothberg teaches *"means for performing a correlation algorithm on the first sequence and the reference sequence, the output of said providing means including a correlation output"* as claimed in claim 14.

It is therefore believed that for the above reasons, a *prima facie* case of obviousness was not established. Therefore, the rejection should be withdrawn.

FODOR (Claims 17-22)

The examiner rejected claims 17-22 under 35 U.S.C. § 103(a) as being unpatentable over Fodor (5,295,525) in view of Rothberg.

The applicant respectfully points out that, like Rothberg, Fodor only discusses computer analysis of chemical reactions, after any hybridization. Neither Rothberg nor Fodor teaches or suggests a machine readable medium causing a machine to implement steps for *"executing an electronic hybridization assay"* as claimed in claim 17 and its dependent claims 18-22 and as defined in the specification. A computer text search of the patent to Fodor was performed, and the term *"electronic hybridization"* was not found to exist in the patent.

Regarding claim 19, neither Fodor nor Rothberg teaches *"wherein the first sequence includes at least one positive and one negative value"* as recited in claim 19. In fact, the examiner never addressed this limitation anywhere in the office action.

Regarding claim 20, neither Fodor nor Rothberg teaches *"performing a correlation algorithm on the first sequence and the reference sequence, the output of said providing means including a correlation output"* as claimed in claim 20.

It is therefore believed that for the above reasons, a *prima facie* case of obviousness was not established. Therefore, the rejection should be withdrawn.

MITSUHASHI (23-25)

The examiner rejected claims 23-25 under 35 U.S.C. § 103(a) as being unpatentable over Mitsuhashi (5,556,749) in view of Rothberg.

Neither Mitsuhashi nor Rothberg teaches a method including *"correlating a first sequence and a reference sequence, the first sequence representing at least one or more subunits of a first molecule and the reference signal representing at least one or more subunits of a second molecule"* as claimed in claim 23 and its dependent claims 24-25 and as defined in the specification. In fact, a computer text search of the patent to Mitsuhashi was performed, and the terms *"correlating"*, *"correlate"*, and *"correlation"* were not found to exist therein. It is therefore believed that the rejection is *prima facie* insufficient.

Regarding claim 25, neither Mitsuhashi nor Rothberg teaches *"said correlating step including a multiply and accumulate operation"* as claimed in claim 25. In fact, the examiner never addressed this limitation anywhere in the entire office action.

It is therefore believed that for the above reasons, a *prima facie* case of obviousness was not established. Therefore, the rejection should be withdrawn.

LEIBOWITZ (Claims 26-30)

The examiner rejected claims 26-30 under 35 U.S.C. § 103(a) as being unpatentable over Leibowitz (5,556,749) in view of Rothberg.

Neither Leibowitz nor Rothberg teaches or suggests *"means for correlating a first sequence and a reference sequence, the first sequence representing at least one or more subunits of a first molecule and the reference sequence representing at least one or more subunits of a second molecule"* as claimed in claims 26-30. In fact, as discussed herein, Rothberg teaches away from such a combination since Rothberg discusses chemical reactions. Furthermore, neither Leibowitz nor Rothberg teaches or suggests *"means for providing an output from said correlating step representative of a relationship between the first and second molecules"* as claimed in claim 26, alone or in combination with the

other elements of claim 26. Thus, the suggested combination does not teach all of the elements as claimed in claim 26. Furthermore, Leibowitz does not suggest correlating two molecular sequences as an application of a correlator, and Rothberg does not teach or suggest using a correlator to perform any of the functions discussed in Rothberg. As a result, there exits no motivation to combine the references. As a result, a *prima facie* showing of obviousness was not set forth.

Regarding claim 28, neither Leibowitz nor Rothberg teaches *"means for executing a multiply and accumulate operation"* as claimed in claim 28. In fact, the examiner never addressed this limitation anywhere in the entire office action.

It should be noted that the applicant was the first to discover that an electronic hybridization assay or the like could be performed using a correlation or correlation-like mathematical algorithm to arrive at a tangible result, for example a correlation output being proportional to a degree of similarity between two molecules. This concept is not found or suggested in the art, either in a single reference or any combination of references or knowledge. Any attempt to use the applicant's disclosure to arrive at the applicant's invention as claimed is impermissible hindsight. It is therefore believed that for the above reasons, a *prima facie* case of obviousness was not established. Therefore, the rejection should be withdrawn.

Objection to the Disclosure

The examiner objected to the disclosure on page 3 based on a minor typographical error. The disclosure has been amended herein to correct the minor typographical error.

Docket No. DTR 112 **PATENT**

CONCLUSION

In light of the foregoing, reconsideration and allowance of the claims is hereby earnestly requested.

Respectfully submitted,
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Docket No. DTR 112 **PATENT**

VERSION WITH MARKINGS TO SHOW CHANGES MADE TO THE CLAIMS

14. (amended) An apparatus as claimed in claim [1] 7, said executing means including means for performing a correlation algorithm on the first sequence and the reference sequence, the output of said providing means including a correlation output.

29. (amended) An apparatus as claimed in claim 26, said means for correlating including at least [one] two or more parallel channels for executing at least [one] two or more correlation algorithms simultaneously, one correlation algorithm for each channel.

30. (amended) An apparatus as claimed in claim [1] 26, at least one of the first sequence and the reference sequence representing a molecule from the group comprising DNA, RNA, a nucleotide, and amino acid, and a protein.

VERSION WITH MARKINGS TO SHOW CHANGES MADE TO THE SPECIFICATION

Paragraph running from bottom of page 2 to top of page 3:

Referring now to FIG. 1, a block diagram of a system for implementing an electronic hybridization assay in accordance with the present invention will be discussed. In operation of hybridization system 100, a first molecule (MOLECULE A) 110 is provided to a sequencing machine (SEQUENCING MACHINE) 112. Sequencing machine 112 determines the sequence of the particular molecular components or residues, referred to generally as subunits, of first molecule 110. For example, first molecule 110 in one embodiment is an oligonucleotide molecule such as DNA or RNA that has a sequence determined by the linear order of its component bases. Such a DNA molecule may comprise, for example, three bases where the molecule is single stranded, or may comprise six base pairs, respectively, where the molecule is double stranded, in which case first molecule 110 has an adenine (A), guanine (G), and a thymine (T) base in sequence. Cytosine (C) may also be one of the bases of a DNA molecule. Thus, where

first molecule 110 is a single stranded molecule, it may have N number of residues where or subunits where N may range from one to infinity, or may have 2N number of residues or subunits, where first molecule 110 is double stranded. Where first molecule 110 is an RNA oligonucleotide, it may include the base uracil (U) instead of thymine. When first molecule 110 is sequenced by sequencing machine 112, sequencing machine 112 provides an output sequence (SEQUENCE A OUTPUT) 114 that is representative of the sequence of the residues, or subunits, of first molecule 110. Sequence output 114 of sequencing machine 112 is provided as an input to an electronic hybridization machine (ELECTRONIC HYBRIDIZATION MACHINE) 116 which is capable of reading and interpreting sequence output 114. In a likewise manner, a second molecule (MOLECULE B) 118 is sequenced by sequencing machine (SEQUENCING MACHINE) 120, which provides a sequence output (SEQUENCE OUTPUT) 122 that is representative of the sequence of second molecule 118. Second molecule 118 may be an oligonucleotide similar to first molecule 110 (e.g., DNA or RNA). Sequence output 122 of sequencing machine 120 is provided to electronic hybridization machine 116 so that an electronic hybridization reaction between first molecule 110 and second molecule 118 is performed electronically rather than chemically. The electronic hybridization reaction, generally referred to as a sequence analysis, performed by electronic hybridization machine 116 is in one embodiment of the invention representative of an actual chemical reaction between the physical forms of first molecule110 and second molecule 118. In a physical world chemical hybridization reaction between first molecule 110 and second molecule 118, the extent to which the two molecules bind to one another is typically indicated with a reporter molecule such as a radioactive of fluorescent reporter molecule. The greater [the greater] the similarity between the two molecules, the greater the amount of binding between the two chemicals, resulting in a fluorescent or radioactive intensity of a signal provided by the reporter molecule. The intensity of the reporter molecule is usually observed by the human eye, or by a detector sensitive to the fluorescence or radioactivity of the reporter molecule. With the present invention, such a hybridization reaction is modeled electronically, in the electronic domain, by electronic hybridization machine 116, which produces a hybridization output (HYBRIDIZATION OUTPUT) 124 representative of information resulting from a hybridization reaction between first

molecule 110 and second molecule 118. The invention is not intended to be limited to hybridization reactions, which are described herein for purposes of illustration. The invention may be expanded or adapted to other types of sequence analysis reactions in accordance with the present invention as described herein.